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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 11/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/773,986	LOUIE-HELM, JENNY, ET AL	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/07/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of IDS, amendment and request for extension of time, all filed 08/22/06. Claim 1 is amended. Claims 1-26 are pending.

Response to Arguments

Rejections not reiterated herein are withdrawn.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

The invention is directed to method for formulating tablet or capsule dosage forms. The deletion of "wherein the dosage form is a tablet" from claim 1 by the amendment broadens to claim to include other than tablet and capsule dosage forms that were not contemplated at the time of filing.

This rejection may be overcome by removing the new matter from the claims.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-11 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Mehra et al. (US 5,830,576) in view of chapter 11-21 of the textbook by Wagner, Biopharmaceutics and Relevant Pharmacokinetics (Drug Intelligence Publications, Hamilton, Il 1971) provided by applicant with the response filed 8/22/06.

Mehra discloses a diuretic formulation that comprises sodium carboxymethyl cellulose or hydroxypropylmethyl cellulose or methylcellulose or alginate or carrageenan (column 3, lines 38-42, Example 19), the formulation is made into tablet dosage form (abstract) and Mehra uses the USP disintegration test to determine the disintegration of the formed granules (column 8, lines 13-20). The formulation further contains lubricants and examples of lubricant used are talc, fatty acid esters and polyethylene glycol (column 4, lines 11-18). Dextran, guar gum, carrageenan , alginates, hydroxypropyl cellulose and carboxymethylcellulose are listed as suspending agents (column 3, lines 38-46). Methylcellulose is listed in instant claim 6 as a hydrophilic polymer. In general, the release profile of dosage forms is a predetermined condition when dosage forms are formulated as is evident in the matrix polymers used with the active agent that would make a dosage form controlled release or immediate release; and in

general in vitro test analysis correlate in vivo pattern of drug release. The excipients used by Mehra in the formulation are the same as those claimed in the instant claims. While Mehra does not specifically disclose correlation between release profile and disintegration and relating disintegration with selecting an optimized controlled release dosage form, Mehra discloses determining tablet disintegration time and effectiveness of excipient for tabletting active agents such as agricultural chemicals (column 8, lines 16-22). Furthermore, the chapters of the book submitted by applicant describes that a decision to formulate dosage forms in the formulary art involves studies of disintegration and dissolution data to correlate in vitro disintegration or dissolution with in vivo processes of drug release and absorption. Applicant supports this in the remarks where applicant states that Wagner recommends employing in vitro disintegration and dissolution processes to design dosages for in vivo use. Therefore, it would have been obvious to one of ordinary skill in the art at the time the time the invention was made to prepare the tablet dosage form of Mehra by determining and obtaining disintegration and/or dissolution data in the decision to formulate the desired dosage form using appropriate excipients/polymer that would further lead to the type of release profile desired. One having ordinary skill in the art would have been motivated to use the appropriate excipients/polymer that would be expected to lead to the desired release profile from the data obtained form the disintegration and/or dissolution studies used to correlate in vitro and in vivo release pattern.

Response to Arguments

5. Applicant's arguments filed 8/22/06 have been fully considered but they are not persuasive.

Applicant argues that a) Mehra does not suggest the claimed process, b) the ordinary skilled artisan would not have been motivated to use the disintegration test of Mehra to prepare controlled release dosage form because disintegration test was not used to test for controlled release dosage forms at the time of the invention and that examiner has used hindsight reasoning to arrive at the claimed invention, and applicant cites chapters 11 (pages 68,69), 12 (page 75 and 79), 13 (second column page 82), 20 (page 125) to support applicant's argument by stating that Wagner shows that disintegration tests were not considered reliable in vitro determinant of in vivo absorption whereas dissolution testing was clearly considered reliable in vitro determinant of in vivo absorption; applicant further cited chapters 711, 701 and 724 of the National Formulary that are applicant submitted, c) the ordinary skilled artisan would have reasonably expected to optimize the dosage form of Mehra to immediate release using disintegration testing.

Response:

Regarding a), while Mehra may not have suggested the claimed process, the various investigations in the Wagner book suggest using disintegration tests to predict in vivo availability of medicaments;

Regarding b), the ordinary skilled artisan would have been motivated by the disclosure of Wagner that using disintegration test and the excipients of Mehra would enable the preparation of sustained release dosage form as according the Mehra as suggested by Wagner. The sections of the book cited by applicant is not conclusive that in vitro disintegration tests failed to predict in vivo availability of pharmaceuticals, the investigation disclosed provides mixed results. For example, Levy says that "USP tablet disintegration test not only failed to predict physiological

unavailability of an enteric coated aspirin tablet but also failed to discriminate between an available enteric coated sodium salicylate tablet and an available enteric coated aspirin tablet." Wagner goes on to state that subsequent to the work of Levy and Holster (1964), Enseals reformulated ASA which had been shown to be physiologically available. Wagner further reports that Levy and Holster found differing results from Morrison and Campbell who found that enteric coated aspirin tablets with disintegration times of 111+ 22.7 minutes were fully available (bottom of page 75, right column to top of left column of page 77). The results on pages 79, 80, 82 and 125 are further testament that a conclusion cannot be made one way or the other. One thing is certain that disintegration-tests are considered in the determination of in vivo availability of medicaments. None of these studies took into consideration of the effect of the excipients on the in vivo availability. Therefore, the fact that some of the studies Wagner linked in vitro disintegration with in vivo availability and also the knowledge that certain excipients give rise to sustained release would motivate the ordinary skilled artisan to expect that the dosage of Mehra would be controlled/sustained release.

Regarding c), Mehra did not disclose immediate release dosage forms. The excipients of Mehra provide sustained or controlled release as is known that alginate is sustained/controlled release excipients from claims 2, 5 and 6 of Groves in US 5,290,559 and from the abstract of Krishnamurthy in US 5,215,758. Therefore, the ordinary skilled artisan would not expect to produce immediate release formulation but rather would reasonably expect that the formulation of Mehra would be controlled/sustained release in view of Wagner where some of the disintegration studies lead to in vivo availability. Furthermore, the only mention of "immediate"

by Mehra is in Example 22 relating where tablets of MCC/urea that do not contain suspending aid settle immediately upon disintegration in water.

Furthermore, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

6. Claims 1-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Friend et al. Franz et al. (US 5,232,704) in view of O'Neil et al. (US 4,704,405) and further in view of chapter 11-21 of the textbook by Wagner, Biopharmaceutics and Relevant Pharmacokinetics (Drug Intelligence Publications, Hamilton, Il 1971) provided by applicant with the response filed 8/22/06.

Franz discloses using in vitro release study in anticipation that the release profile of prepared dosage formulation would be sustained according to the in vitro release study data (column 9, lines 7-30; column 12, lines 25-50; abstract); the formulation comprises active ingredient such as prostaglandin and non-steroidal anti-inflammatory drug (column 3, lines 15-33; column 4, lines 4-10), hydroxypropyl methylcellulose, carboxymethylcellulose and PVP or polyethylene glycol (column 5, lines 15-33). Frantz administers the formulation to subject in the fed state and once daily (column 14, 36-44).

Franz disclose release profile of capsules of anti-inflammatory agents determined by disintegration. Franz does not disclose a tablet. O'Neil disclose NSAID's formulated as tablet (abstract; column 2; column 3, lines 11-15). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare and use the NSAID containing composition for administration to a subject in the fed state. It is known in the art and as disclosed by O'Neil that NSAID's can be formulated as tablets.

The combined tablet formulation of Franz and O'Neil does not specifically state that disintegration data can be used to predict in vivo availability of medicaments. However, the chapters of the book submitted by applicant describes that a decision to formulate dosage forms in the formulary art involves studies of disintegration and dissolution data to correlate in vitro disintegration or dissolution with in vivo processes of drug release and absorption. Applicant supports this in the remarks where applicant states that Wagner recommends employing in vitro disintegration and dissolution processes to design dosages for in vivo use. Therefore, it would have been obvious to one of ordinary skill in the art at the time the time the invention was made to prepare the tablet dosage form of O'Neil and Franz by determining and obtaining disintegration and/or dissolution data in the decision to formulate the desired dosage form using appropriate excipients/polymer that would further lead to the type of release profile desired. One having ordinary skill in the art would have been motivated to use the appropriate excipients/polymer that would be expected to lead to the desired release profile from the data obtained form the disintegration and/or dissolution studies used to correlate in vitro and in vivo release pattern.

It would have therefore been a motivation to prepare and use composition of Franz in tablet form as disclosed by O'Neil and as suggested by Wagner with the expectation that the formulation would release the active agent according to disintegration profile in a sustained manner.

Response to Arguments

7. Applicant's arguments filed 8/22/06 have been fully considered but they are not persuasive.

Applicant had presented arguments against a rejection under 35 USC 102. But there was no rejection under 35 USC 102 in the last office action.

Applicant argues that Franz does not use disintegration data in the manner suggested by Wagner and that O'Neil does not correct the deficiency of Franz.

Response to arguments:

Here, Wagner suggests use of disintegration to predict in vivo availability. While the investigations support either failure of disintegration data to support bioavailability or the success of disintegration data to support in vivo bioavailability, there is nonetheless suggestion of successful correlation of in vitro disintegration with in vivo bioavailability and the use of sustained release excipients would both enable ordinary skilled artisan to expect the combined dosage form of Franz and O'Neil to be sustained/controlled.

No claim is allowed.

8. Applicant's amendment and the submission of the Wagner document necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE**

FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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